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FORUM EDITORIAL

Antioxidants and Public Health

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THE ROLE OF ANTIOXIDANTS in nutritional systems was proposed in 1927 when Henry Mattill used the term "antioxidizer" to describe the action of dietary factors that prevented oxidation (11). The concept of antioxidation, especially as it related to vitamin E, emerged as being important in physiological functions such as reproduction. Additional roles for antioxidants have subsequently become apparent, and the antioxidant capacity of the diet is now considered to be a significant contributor to optimal health.

Numerous controlled intervention trials have explored the role of antioxidants (alone or in combinations) in the prevention of chronic diseases, mainly cardiovascular disease and cancer. The results have been equivocal (9); nevertheless the current evidence continues to support the physiological relevance of antioxidants and adds weight to recommendations that the dietary intake of antioxidants is desirable. The search for different types and sources of antioxidants and the elucidation of their mechanisms of action remain subjects of great interest.

Vegetarian diets are increasingly popular as a lifestyle choice, and some of the benefits associated with this dietary pattern can be attributed to a lower intake of saturated fat and cholesterol and a higher intake of dietary fiber as compared with some omnivorous diets. However, plant-based diets additionally contribute substantial quantities of bioactive compounds such as the antioxidant vitamins and also phytonutrients. The review by Benzie and Wachtel-Galor (2) in the current Forum issue presents evidence for the health benefits of vegetarian diets and ascribes the effects to the intake of antioxidants, which are capable of modulating redox tone and signaling. Vegetarian diets offer numerous nutritional and health benefits (4), and Benzie and Wachtel-Galor conclude that, despite the dearth of information on mechanisms of action, there is sufficient evidence for public health policy makers to promote a plant-rich diet.

The biological effects of specific phytonutrient preparations have been investigated. For instance, tea extracts and their constituent catechins are reported to produce a range of favorable health outcomes, including enhanced loss of abdominal fat mass (7). Favorable effects have been reported also for resveratrol, which under controlled conditions was shown to increase longevity in mice (1). The landmark study by Baur *et al.* (1) presented evidence for a role for resveratrol in changing the pattern of gene expression in mice and, more specifically, in shifting the profile of gene expression in animals fed a high-calorie diet to be similar to control animals. The review in the present Forum by Wood *et al.* (12) provides further evidence for the role of resveratrol in cellular metabolism via its ability to reduce oxidative stress in airway disease. The authors propose that resveratrol is a potentially useful agent in the management of airway disease and other chronic diseases. The mechanism of action includes antioxidation, but resveratrol could also act by altering cellular signaling events that reduce inflammation. Resveratrol is reported to occur in large quantities in grapes and could be partly responsible for the health benefits of moderate consumption of wine.

Short-term or acute studies have shown that the consumption of foods with a high polyphenolic content and antioxidant capacity *in vitro* (e.g., tea or berries) leads to an increase in the polyphenol concentration in the circulation (10). However, very few clinical trials have been carried out to determine the effect of polyphenol-rich foods on biomarkers of chronic disease or antioxidant status. In this Forum issue, Yang *et al.* (13) report on the results of a trial in humans in which subjects consumed diets with added lupin kernel, a legume that is traditionally used as a component of animal feed. This commodity is rich in polyphenols and has potential as a staple food for humans. The outcome of the trial is that consumption of lupin produces a lowering in blood pressure, and positive correlations were reported between blood pressure, cholesterol concentrations, and urinary F2-isoprostanes. The trial demonstrates that a single food item as part of a varied diet can elicit favorable metabolic changes, which are potentially additive with benefits derived from further dietary adjustments, for example, an increase in the intake of dietary fiber.

Zinc is a nutrient with numerous functions including the regulation of gene expression (3). Zinc deficiency is common due to its low nutritional bioavailability, ironically caused by the consumption of phytic acid, a phytochemical constituent of cereals (8). Zinc deficiency affects a large percentage of the world's population, and much of the research on zinc has focussed on its effects on growth and infection. In this Forum issue, Foster and Samman (5) evaluate emerging roles for zinc in redox metabolism. Zinc ions are integral to the activities of superoxide dismutase and metallothionein, both of which protect against an accumulation of reactive species in cellular systems. Intracellular sequestration of zinc by metallothionein, or its transport via zinc transporters, can determine the localization of zinc and regulate the equilibrium of active-inactive enzymes. This process can potentially influence

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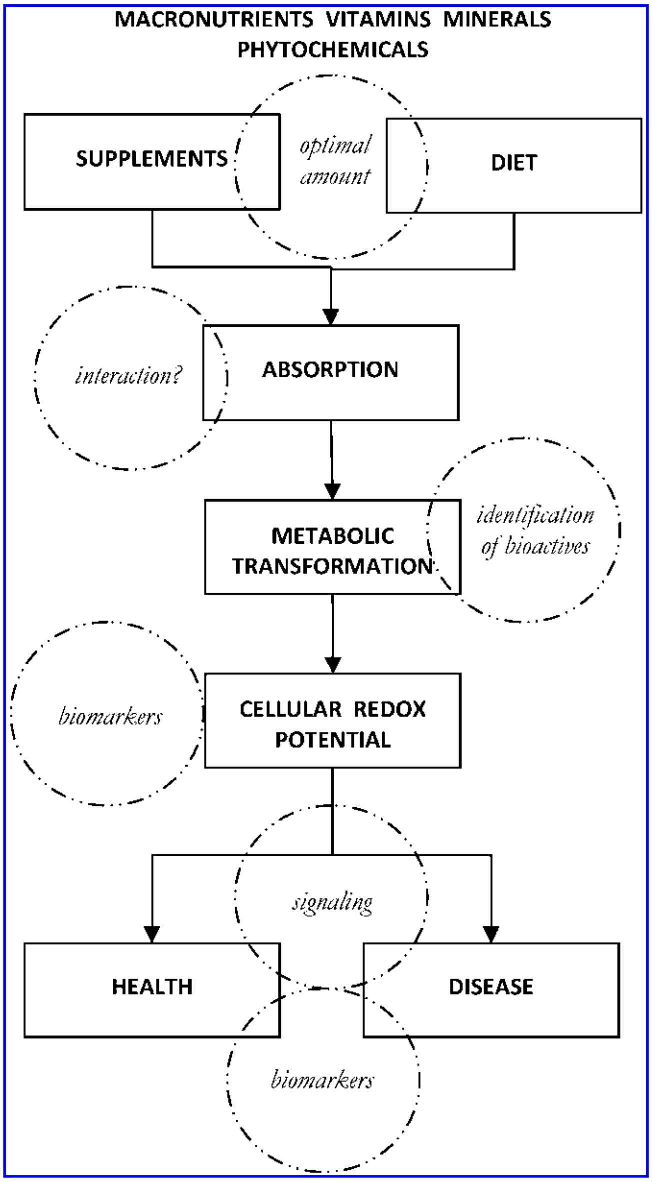

FIG. 1. Antioxidants in the diet–disease relationship. Gaps in knowledge exist in identifying the optimal dose of nutrients in the diet or as supplements, subsequent interactions, and metabolic transformations. The impact on cellular redox potential and signaling and their assessment remain controversial.

signaling molecules that regulate gene expression. Moreover, zinc itself acts as a signaling molecule and may function to extend the signaling capacity of other nutrients such as calcium and magnesium. The interactions between zinc and other nutrients, including the potential chelation of zinc by some phytonutrients, suggests that the therapeutic doses (or levels of dietary intake) of zinc have to be carefully considered to ensure maximal physiological benefit.

Endogenously generated metabolites can play a potentially important role in modifying disease outcomes. Gieseg *et al.* (6) has shown that the synthesis of 7,8-dihydroneopterin, which is triggered by a metabolic cascade in T helper (Th1) cells, leads to the preservation of intracellular glutathione concentrations and effective scavenging of intracellular oxidants. An interaction with zinc metabolism is plausible given that oxidative stress induced by zinc deficiency leads to a shifting of the balance of Th1/Th2 cells toward decreased synthesis of Th1 cells.

Future Directions

As mentioned on a number of occasions in this issue, further research into the mechanistic actions of phytochemicals is required (Fig. 1), particularly the characterization of the actions beyond antioxidation. Although good progress has been made in the identification of the naturally occurring phytochemicals, real gaps exist in our knowledge of the biological transformations that take place in humans after these compounds are consumed. Knowledge of synergy and/or antagonism that may exist between phytonutrients and the recognized nutrients, especially trace elements, is also in its infancy, as is our understanding of the biochemical interactions that take place during their metabolism. Further research is needed in humans, particularly clinical trials that utilize the principles of evidence-based medicine.

References

1. Baur JA, Pearson KJ, Price NL, Jamieson HA, Lerin C, Kalra A, Prabhu VV, Allard JS, Lopez-Lluch G, Lewis K, Pistell PJ, Poosala S, Becker KG, Boss O, Gwinn D, Wang M, Ramaswamy S, Fishbein KW, Spencer RG, Lakatta EG, Le Couteur D, Shaw RJ, Navas P, Puigserver P, Ingram DK, de Cabo R, and Sinclair DA. Resveratrol improves health and survival of mice on a high-calorie diet. *Nature* 444: 337–342, 2006.
2. Benzie IFF and Wachtel-Galor S. Vegetarian diets and public health: biomarker and redox connections. *Antioxid Redox Signal* 13: 1575–1591, 2010.
3. Cousins RJ, Aydemir TB, and Lichten LA. Transcription factors, regulatory elements and nutrient-gene communication. *Proc Nutr Soc* 69: 91–94, 2010.
4. Craig WJ and Mangels AR. American Dietetic Association. Position of the American Dietetic Association: vegetarian diets. *J Am Diet Assoc* 109: 1266–1282, 2009.
5. Foster M and Samman S. Zinc and redox signaling: perturbations associated with cardiovascular disease and diabetes mellitus. *Antioxid Redox Signal* 13: 1549–1573, 2010.
6. Gieseg SP, Amit Z, Yang YT, Shchepetkina A, and Katouah H. Oxidant production, oxLDL uptake, and CD36 levels in human monocyte–derived macrophages are downregulated by the macrophage-generated antioxidant 7,8-dihydroneopterin. *Antioxid Redox Signal* 13: 1525–1534, 2010.
7. Maki KC, Reeves MS, Farmer M, Yasunaga K, Matsuo N, Katsuragi Y, Komikado M, Tokimitsu I, Wilder D, Jones F, Blumberg JB, and Cartwright Y. Green tea catechin consumption enhances exercise-induced abdominal fat loss in overweight and obese adults. *J Nutr* 139: 264–270, 2009.
8. Prasad AS, Mialea A Jr., Farid Z, Sandstead HH, and Schulert AR. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism, and hypognadism. *J Lab Clin Med* 61: 537–549, 1963.
9. Tribble DL. Antioxidant consumption and risk of coronary heart disease: emphasis on vitamin C, vitamin E, and

β-carotene: a statement for healthcare professionals from the American Heart Association. *Circulation* 99: 591–595, 1999.
10. van het Hof KH, Wiseman SA, Yang CS, and Tijburg LB. Plasma and lipoprotein levels of tea catechins following repeated tea consumption. *Proc Soc Exp Biol Med* 220: 203–209, 1999.
11. Wolf G. The discovery of the antioxidant function of vitamin E: the contribution of Henry A. Mattill. *J Nutr* 135: 363–366, 2005.
12. Wood LG, Wark PAB, and Garg ML. Antioxidant and anti-inflammatory effects of resveratrol in airway disease. *Antioxid Redox Signal* 13: 1535–1548, 2010.
13. Yang X, Croft KD, Lee YP, Mori TA, Puddey IB, Sipsas S, Barden A, Swinny E, and Hodgson JM. The effects of a lupin-enriched diet on oxidative stress and factors influencing vascular function in overweight subjects. *Antioxid Redox Signal* 13: 1517–1524, 2010.

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1. M. Stoia, S. Oancea. 2012. Workplace Health Promotion Program on Using Dietary Antioxidants (Anthocyanins) in Chemical Exposed Workers. *Procedia Engineering* **42**, 2176-2186. [CrossRef]
2. Hyo Jung Kim, Mi-Kyung Sung, Jong-Sang Kim. 2011. Anti-inflammatory effects of glyceollins derived from soybean by elicitation with Aspergillus sojae. *Inflammation Research* **60**:10, 909-917. [CrossRef]